

Clinical Bottom Line

Benefits:

By Indication (Risk Group)

- For women with current singleton pregnancies and a history of spontaneous preterm birth who are treated with progesterogens:

◇ The risk of preterm birth (prior to 37 weeks) is reduced by one-third (absolute risk reduction = 9.4%; NNT* = 11)

◇ Neonatal mortality risk is reduced by half (absolute risk reduction = 1.7%; NNT = 59)

◇ Birth weights may increase, but the estimated effect is not statistically significant

- In women with a short cervix:

◇ Progesterone treatment reduces the risk of preterm birth, but the size of the effect is not clearly established (an absolute risk reduction of 9% and 15% in two trials)

◇ 17P is not effective in reducing risk of PTB

- In women with multiple gestations (twin or triplet), there is no benefit of 17P use in women without a history of a prior preterm birth:

◇ Birth is not delayed

◇ Birth weights are not improved

◇ The evidence is insufficient to estimate effects on neonatal mortality rates

- The evidence is insufficient for all other indications, including women with symptoms of preterm labor, and for populations with varied risk factors

- The evidence about benefits of progesterogens for other maternal, fetal, neonatal, and perinatal outcomes (e.g., conditions of prematurity, NICU† admissions) is insufficient to guide clinical decision making

By Formulation/Route of Administration

- When assessed by routes of administration alone (injected and vaginal), all formulations reduce the risk of preterm birth, but none reduce neonatal mortality rates

- Without head-to-head trials, the evidence is insufficient to determine if formulation and administration route are associated with different maternal or fetal outcomes or adverse effects

Adverse Effects

Safety of Progesterogens

- Study withdrawal rates (a measure of tolerability) were similar for treated and control groups
- The most common adverse effects were related to route of administration (injection site discomfort, vaginal irritation)
- The evidence is insufficient to understand the short- and long-term maternal and fetal adverse effects

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What to do to prevent a **PRETERM BIRTH** 17P and Vaginal Progesterone

A Guide for Providers



UWNQC

Utah Women & Newborns Quality Collaborative

What is 17P?

- 17 alpha-hydroxyprogesterone caproate (17P) is a synthetic form of progesterone that has been shown to reduce the recurrence of preterm birth (PTB) for women with singleton gestations that have a history of previous PTB
- A prescription medication, 17P is administered through weekly injections beginning at 16-24 weeks until delivery
- Women with a previous history of PTB are more likely to have another preterm infant compared to women who have not
- Each year, approximately, 30,000 pregnant women meet criteria and are considered eligible for 17P
- Studies show that administering 17P to an eligible woman reduces the chance of having another PTB by 33 percent
- Although a woman may still deliver a few weeks early, women who use 17P are more likely to carry the pregnancy at least one week longer than those who did not take 17P
- With no other safe and tested technologies available to effectively prevent PTB, 17P provides the strongest solution to halting premature birth in eligible women
- The U.S. PTB rate in 2013 was 11.4 percent, highest of all high-resource countries
- There is marked racial disparity in preterm births, contributing to large disparities in infant health outcomes
- Increasing the availability and access to 17P is a critical step in improving PTB rates and reducing disparities

Who is an appropriate candidate for 17P?

Women eligible for 17P should meet the following criteria:

- Have a history of a previous singleton spontaneous preterm birth (*see definition at bottom of page) between 20 and 36+6/7 weeks gestation
- Have a current singleton pregnancy
- Initiate treatment between 16 and 21+6/7 weeks gestation
- If an eligible woman presents to prenatal care late, 17P may be initiated as late as 23+6/7 weeks
- Continue treatment until 36 completed weeks gestation

Currently, studies have not demonstrated that 17P is an effective intervention for the prevention of preterm birth in other pregnant women. The use of 17P is **NOT** appropriate for women with the following conditions:

- Multi-fetal pregnancy
- A short cervix and no prior preterm birth
- A previous medically indicated preterm birth

Who is an appropriate candidate for vaginal progesterone?

Vaginal progesterone is an appropriate intervention for women who are diagnosed with a short cervix during pregnancy. There are some data about the use of vaginal progesterone in women with a previous spontaneous preterm birth (*see definition below) but the evidence for the efficacy of this treatment is limited. Treatment with vaginal progesterone may be considered in women who do not tolerate 17P injections.

**Spontaneous preterm birth:* Any preterm delivery that follows presentation as labor, preterm premature rupture of membranes (PPROM), advanced cervical dilation/cervical insufficiency or abruption/vaginal bleeding.

What are the risks of 17P?

Studies show that 17P is safe and that there are no serious side effects for the mother or the baby. Results also demonstrate that there is no increase in the rate of birth defects for infants whose mothers used 17P during pregnancy. One study continues to follow infants into childhood and has observed no increased risk for birth defects and other health problems.

What are potential side effects of Progestogens?

Side effects are very rare. If side effects do occur, they are most commonly related to the route of administration and include soreness, swelling, itching, or bruising at the site of the injection or vaginal irritation.

How are Progestogens prescribed?

| MEDICATION | 17P Makena™ or Compounded | Natural progesterone | Crinone Gel 8% |
|-------------|---|--|---------------------------------------|
| INDICATION | Prior spontaneous PTB in singleton | Short Cervix or Prior spontaneous PTB in singleton | Short cervix |
| DOSAGE | 250 mg IM weekly | 200 mg suppositories per vagina nightly | 90 mg/1 applicator per vagina nightly |
| START | 16-20 wks gestation is ideal, may start as late as 23+6/7 wks | Upon diagnosis | Upon diagnosis |
| STOP | 37 wks gestation | 37 wks gestation | 37 wks gestation |
| MISSED DOSE | Give dose as soon as possible (5-9 day interval pre-ferred) | Give dose as soon as possible | Give dose as soon as possible |

How to store Progestogens:

All formulations may be kept at room temperature. For best results, 17 P should be kept in a dry place away from direct heat and sunlight. If the medication looks cloudy it may have been stored for too long.

Availability of Progestogens:

There are several Compounding Pharmacies in Utah that dispense the Compounded 17P. Refer to UWNQC.org for pharmacy information.

Billing questions:

Currently in Utah, Medicaid covers 17P. Refer to UWNQC.org for billing questions.

